REMARKS

Claims 1, 3-5, 7-10, 12-13 and 15-18 are pending in this application. Claims 2, 6, 11 and 14 were cancelled. In the outstanding Office Action, claim 1 was objected to because of informalities. Claims 1, 3-5, 7-10, 12-13 and 15-16 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Claims 1, 4-5, 7, 10, 13, and 16-18 were rejected under 35 U.S.C. §103(a) as being unpatentable over Phipps et al. U.S. Patent No. 5,533,971 ("Phipps") in view of the Table of pKa and PI Values for Amino Acids and in further view of Petelenz et al. U.S. Patent No. 4,752,285 ("Petelenz"). Claims 1, 3, 10 and 12 were rejected under 35 U.S.C. §103(a) as being unpatentable over Phipps in view of the Table of pKa and PI Values for Amino Acids, in further view of Petelenz, and in further view of the lidocaine record in the Merck index. Claims 1, 3, 9-10 and 12 were rejected under 35 U.S.C. §103(a) as being unpatentable over Phipps in view of the Table of pKa and PI Values for Amino Acids, in further view of Petelenz, and in further view of Parkinson et al. U.S. Patent Application Publication No. 2003/0023228 ("Parkinson"). Claims 1 and 8 were rejected under 35 U.S.C §103(a) as being unpatentable over Phipps in view of the Table of pKa and PI Values for Amino Acids, in further view of Petelenz and in further view of Hsu et al U.S. Patent Publication No. 2003/0161870 ("Hsu"). Claims 10 and 15 were rejected under 35 U.S.C §103(a) as being unpatentable over Phipps in view of the Table of pKa and PI Values for Amino Acids, in further view of Petelenz and in further view of the Grain Processing Corporation WATERLOCK Superabsorbent Polymers reference.

Claims 3 and 12 have been amended to correct a clerical error in the drawing of the chemical structure of dexamethasone. Claims 1, 4, 10 and 17 have been amended. Claims 19-22 have been added. All amendments are fully supported by Applicants' specification as originally filed (see, e.g., paragraphs 0021-0025), and thus no new matter is added. Applicants respectfully traverse the rejections.

Objection to claim 1

The Examiner has objected to claim 1 because of the following informalities: "the recitation of the claimed device includes a living subject as a component implicitly present" (Office

Action, page 2). The preamble of claim 1 has been amended to recite "An iontophoretic device for transdermally delivering a medicament when applied to a living subject's body" (emphasis added). In light of this amendment, Applicants respectfully request the withdrawal of this objection.

Claim rejections under 35 U.S.C. §112, first paragraph

Claims 1, 3-5, 7-10, 12-13 and 15-16 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner has stated that "Claims 1 and 10 recite 'a second electrode in direct electrical communication with a living subject's body'. This recitation has no basis in the disclosure as filed…" (Office Action, page 3). Claims 1 and 10 have been amended to remove this element, and thus Applicants respectfully request the withdrawal of these rejections.

Claim rejections under 35 U.S.C. §103(a)

Claims 1, 3-5, 7-10, 12-13, and 15-18 were rejected under 35 U.S.C. §103(a) as being unpatentable over varying combinations of Phipps, the Table of pKa and PI Values for Amino Acids, Petelenz, the lidocaine record in the Merck index, Parkinson, Hsu and the Grain Processing Corporation WATERLOCK Superabsorbent Polymers reference. Applicants respectfully traverse these rejections.

As amended, claim 1 provides an iontophoretic device for transdermally delivering a medicament when applied to a living subject's body. The device includes a buffering agent associated with a polymeric gel matrix; wherein the buffering agent maintains pH of the gel matrix from approximately 4.1 to approximately 4.9 and is present in a concentration of greater than about 1.0 M. The device further includes a viscosity enhancer associated with the polymeric gel matrix, a rehydrating agent associated with the polymeric gel matrix, a medicament associated with the polymeric gel matrix. and an active electrode assembly associated with the polymeric gel matrix, wherein the active electrode assembly includes a first electrode in electrical communication with medicament ions in the polymeric gel matrix.

As amended, claim 10 provides a method for treating an affected area of a living subject's body. The method includes associating a medicament with a matrix in an iontophoretic delivery

device and providing an effective amount of pH buffering agents to the matrix, wherein the buffering agents maintain the pH of the matrix from approximately 4.1 to approximately 4.9 and are present in a concentration of greater than about 1.0 M. The method further includes providing a viscosity enhancer to the matrix. adding a rehydrating agent to the matrix, and associating an active electrode assembly with the matrix, wherein the active electrode assembly includes a first electrode in electrical communication with medicament ions in the polymeric gel matrix. The method also includes positioning at least a portion of the iontophoretic delivery device on the affected area of a living subject and iontophoretically delivering the medicament to the affected area of the living subject to minimize skin inflammation.

Applicants respectfully submit that none of the cited references teach or suggest several of the features of the device of claim 1 and the method of claim 10. For example, none of the cited references teach or suggest, at least, including a buffering agent that maintains the pH of a gel matrix from approximately 4.1 to approximately 4.9 and is present in a concentration of greater than about 1.0 M. Instead, Phipps teaches that "the buffer concentration in the anodic reservoir will range from about 0.01 M to about 1.0 M. Preferably, the buffer concentration will be about 0.01 M to about 0.50 M. More preferably, the buffer concentration will be about 0.01 M to about 0.20 M" (Phipps, col. 14, lines 53-57). Petelenz explicitly teaches against the use of buffers in an iontophoretic system entirely, stating that "The introduction of buffers is found to defeat some of the important useful features of iontophoresis" (Petelenz, col. 4, lines 11-12). Instead, Petelenz teaches that "the iontophoretic techniques of the present invention maintain safe pH levels without the addition of buffering ions" (Petelenz, col. 5, lines 58-60).

Parkinson also fails to teach or suggest a buffering agent that maintains the pH of a gel matrix from approximately 4.1 to approximately 4.9 and is present in a concentration of greater than about 1.0 M. Rather, Parkinson describes embodiments in which the pH of an iontophoretically-delivered composition is "adjusted to 7.0-8.5; with sodium hydroxide and/or citric acid added, if needed" (Parkinson, paragraph 0018) or is "near isotonic and buffered to near pH 7.4" (Parkinson, paragraph 0019). Hsu also fails to teach or suggest such a buffering agent, and instead teaches that "the pH at the body surface in contact with a formulation or drug delivery system of the invention should be in the range of approximately 8.0 to 13, preferably in the range of about 8.0 to 11.5, more

preferably about 8.5 to 11.5" (Hsu, paragraph 0050). With respect to the Table of pKa and PI Values for Amino Acids, the lidocaine record in the Merck index, and the Grain Processing Corporation WATERLOCK Superabsorbent Polymers reference, Applicants assert that these references simply do not teach or suggest the use of a buffering agent that maintains the pH of a gel matrix from approximately 4.1 to approximately 4.9 and is present in a concentration of greater than about 1.0 M.

For at least the reasons described above, none of the cited references, alone or in combination, teaches or suggests, at least, a buffering agent that maintains the pH of a gel matrix from approximately 4.1 to approximately 4.9 and is present in a concentration of greater than about 1.0 M. Accordingly, Applicants respectfully request the withdrawal of the rejection of claims 1 and 10. Claims 3-5, 7-9, 12-13 and 15-16 depend from at least one of claims 1 and 10, and are thus allowable for at least the reasons described above, and due to the additional features recited therein.

As amended, claim 17 provides an iontophoretic device for transdermally delivering a medicament when applied to a patient's skin. The device includes a buffered polymeric gel matrix positionable adjacent to a patient's skin; a viscosity enhancer associated with the polymeric gel matrix, wherein the viscosity enhancer comprises hydroxy ethyl cellulose having a concentration of less than about 0.3% by weight; and a rehydrating agent associated with the polymeric gel matrix, wherein the rehydrating agent comprises sodium polyacrylate having a concentration of less than about 0.6% by weight and polysorbate 20. The device further includes a medicament included in the polymeric gel matrix; and an electrode assembly associated with the polymeric gel matrix, wherein the electrode assembly includes a first electrode adapted to receive the medicament from the polymeric gel matrix and deliver the medicament to the patient's skin.

Applicants respectfully submit that none of the cited references teach or suggest several of the features in the device of claim 17, including a viscosity enhancer associated with the polymeric gel matrix, wherein the viscosity enhancer comprises hydroxy ethyl cellulose having a concentration of less than about 0.3% by weight; and a rehydrating agent associated with the polymeric gel matrix, wherein the rehydrating agent comprises sodium polyacrylate having a concentration of less than about 0.6% by weight and polysorbate 20.

Phipps does not teach or suggest the desirability of enhancing the viscosity of a iontophoretic device composition. Instead, Phipps describes the inclusion of hydrophilic polymers which "preferably represent from a few percent up to about 50 percent by weight" (Phipps, col. 17, lines 14-15) and lists examples including "WATER LOCK … which is a starch-graft-poly(sodium acrylate-co-acrylamide) polymer" and "hydroxyethyl cellulose" (Phipps, col. 17, lines 24-27). Phipps also states that "the reservoirs may also contain other conventional materials such as water, permeation enhancers, dyes, pigments, inert fillers, and the like" (Phipps, col. 17, line 67-col. 18, line 3). With respect to permeation enhancers, the Examiner has acknowledged that Phipps "does not teach particular examples of chemicals that could serve in this role" (Office Action, page 10) and has stated that "Hsu et al. teach that a variety of compounds are used in the art of drug delivery to enhance skin permeability that includes polysorbate 20" (Office Action, page 10).

Thus, combining these teachings of Phipps and Hsu would yield an iontophoretic device composed of:

- polysorbate 20, and
- at least a few percent by weight of hydrophilic polymers that could include sodium polyacrylate and hydroxy ethyl cellulose.

However, such a composition does not describe the combination of elements recited in claim 17, which comprises:

- polysorbate 20, and
- sodium polyacrylate having a concentration of less than about 0.6% by weight and hydroxy ethyl cellulose having a concentration of less than about 0.3% by weight.

Thus, the combination of Phipps and Hsu fails to teach or suggest the iontophoretic device recited in claim 17. Petelenz fails to mention any rehydrating agents or viscosity enhancers, including any of polysorbate 20, sodium polyacrylate and hydroxy ethyl cellulose. Parkinson states that "the solution may also contain supplemental agents, such as electrolytes, stability additives, medicament preserving additives, pH regulating buffers, etc." (Parkinson, paragraph 0038), but fails to teach or suggest the use of a rehydrating agent and a viscosity enhancer, nor any particular supplemental agents. The Table of pKa and PI Values for Amino Acids, the lidocaine record in the Merck index, and the Grain Processing Corporation WATERLOCK Superabsorbent Polymers

reference simply do not teach or suggest the use of a rehydrating agent and a viscosity enhancer as recited in claim 17.

For at least the reasons described above, none of the cited references, alone or in combination, teaches or suggests at least a rehydrating agent and a viscosity enhancer as recited in claim 17. Accordingly, Applicants respectfully request the withdrawal of the rejection of claim 17. Claim 18 depends from claim 17, and is thus allowable for at least the reasons described above, and due to the additional features recited therein.

CONCLUSION

In view of the above amendment and remarks, Applicants believe the pending application is in condition for allowance.

Applicants believe no fee is due with this response other than as reflected on the enclosed transmittal. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. ACIZ-148-101 from which the undersigned is authorized to draw.

Dated: November 9, 2009

Respectfully submitted,

By /Laura Zager/

Laura Zager
Registration No.: 64,813
ROPES & GRAY LLP
One International Place
Boston, Massachusetts 02110
(617) 951-7000
(617) 951-7050 (Fax)
Attorneys/Agents For Applicants